REMARKS

Claims 1-21, 36-38, and 41-45 are pending in the above-identified patent application. Claims 22-35, 39, and 40 were canceled upon Examiner's restriction requirement, with traverse, and the right to file a divisional application was reserved.

Claims 2, 7, 12, and 41 have been deleted to obviate an enablement rejection based on references therein to an Mpf cell line designated by ATCC accession number 1656-CRL, in accordance with the Examiner's recommendations in the Advisory Action of October 24, 2000 in Patent Application No. 09/040,103.

Claims 46-70 are new, of which Claim 46 is independent. Support for new independent Claim 46 is found, for example, in the Specification at page 6, line 25 to page 7, line 31. The dependent claims track the claims dependent on Claim 1. No new matter is introduced by these claims.

Accordingly, upon entry of the Preliminary Amendment, claims 1, 3-6, 8-11, 13-21, 36-38, and 41-70 will be pending and under examination in the subject application.

I. Rejection under 35 U.S.C. § 102(e)

Claims 1, 3-6, 8-11, 13-21 and 36-38 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,871,997 to Rother *et al.* ("Rother").

Amended Claim 1 is directed to a method of preparing a stable retroviral packaging cell line to produce human serum-resistant RVP. The first step provides that one or more packaging vectors are introduced into a non-primate mammalian cell line that (1) exhibits substantially no hybridization to a Moloney-MLV retrovirus *gag*, *pol* or *env* probe; and (2) is capable of producing human-serum-resistant RVP. Each remaining claim depends directly or indirectly from amended Claim 1, and thus includes these aspects of the cell line.

Rother does not disclose any such cell line and therefore does not anticipate the invention as claimed. Rother is directed to cell lines which lack galactose alpha (1,3) galactosyl epitopes, *i.e.*, α-galactosyl negative cells or cells that have been modified and/or selected in order to obtain cells that do not express galactose alpha (1,3) galactosyl epitopes (*see, e.g.*, Col. 9, Lines 19-23). All cell lines disclosed by Rother that are useful for production of serum resistant RVP are α-galactosyl negative, either because they inherently do not express galactose alpha (1,3) galatosyl epitopes, or because they have been treated, for example with glycosylation inhibitors, to inhibit such expression. The Examiner states that the rejection is predicated on the non-primate CHO and BHK cells recited by Rother, which, it is asserted, inherently have α-galactosyl on the cell surface and fall within the claimed invention. Contrary to the Examiner's assertion, non-primate CHO and BHK cells disclosed as useful by Rother do not have α-galactosyl on the cell surface. Rother teaches this is a necessary feature of cell lines making human-serum-resistant RVP. Rother is unconcerned with any other aspect of the disclosed cells. Since the presence or absence of α-galactosyl on the cells of the instantly claimed invention is irrelevant, Rother teaches away from the instantly claimed invention.

Rother is unconcerned with retroviral sequences that are or might be present in cell lines useful for making human-serum-resistant RVP. In response to the Examiner's comment that he could find no evidence in the art that CHO or BHK cells have endogenous retroviruses, the Applicant directed his attention to Lie *et al.* (1994) "Chinese hamster ovary cells contain transcriptionally active full-length type C proviruses" *Virology* 68:7840-7849 as evidence that CHO cells have endogenous retrovirus sequences capable of hybridizing to a Moloney-MLV retrovirus probe. The applicant further noted that the ML2G sequences used as a probe are homologous to Moloney-MLV retrovirus sequences. Lie further provides evidence that BHK cells contain endogenous retrovirus sequences which hybridize to the

same probe under stringent washing conditions, though the endogenous BHK retroviral sequences are more distantly related than the CHO retroviral sequences. Thus, the Applicant has provided evidence that both the BHK and CHO cell lines harbor endogenous retroviral sequences which hybridize to a murine MoLV probe.

Applicant respectfully asserts that this evidence is more than sufficient, especially in view of the Examiner's rejection based on an inability to find evidence in the art that CHO and BHK cells have endogenous retroviruses. In effect, the Examiner's position is that it is inherent that non-primate mammalian cells exhibit substantially no hybridization to a Moloney-MLV retrovirus probe.

To support an anticipation rejection based on inherency, an examiner must provide factual and technical grounds establishing that the inherent feature *necessarily* flows from the teachings of the prior art. *See Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. Int. 1990); *see also In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323,326 (C.C.P.A. 1981) (holding that inherency must flow as a necessary conclusion from the prior art, not simply a possible one). The Examiner chose two cell lines conveniently present in the prior art, but provided no evidence that an element of the claimed invention was necessarily present. Indeed, the Examiner has conceded that CHO cells exhibit hybridization to a Moloney-MLV probe. Thus, the Applicant respectfully points out that the Examiner has not met the burden necessary to support the anticipation rejection.

Applicant asserts that the rejection is improper and respectfully requests that it be withdrawn.

II. Rejection under 35 U.S.C. § 112, first paragraph

Claims 2, 7, 12 and 41 have been rejected for non-enablement in view of their specific reference to cell lines deposited at the ATCC for which there is no assurance of unrestricted access. Claims 2, 7, 12 and 41 reciting the ATCC Accession Number are now cancelled

according to the Examiner's advice, as Mpf cells are readily available from the ATCC and other sources. The rejection is moot. Claims 42-45 recite the same cell line, but without reference to a specific ATCC deposit.

III. Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-21, 36-38 and 41-45 stand rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner asserts that because the skilled artisan would not know what sequences to select in naking a "Moloney MLV retrovirus probe," the length and type of probes must be specified. Accordingly, Claim 1 is amended to recite "Moloney-MLV retrovirus *gag*, *pol* and *env* probes." Thus, probes are selected from the regions of the Mo-MLV genome which share homology with other retroviruses. Sequences of the *gag*, *pol* and *env* genes of Mo-MLV have long been know in the art and the preparation and use of such proves to detect an endogenous retrovirus sequence is routine.

The Examiner has asserted that the phrase "substantially no hybridization" is totally unclear, and that the use of the term "substantially" to modify a negative or null term reners the claims unclear. The Applicant disagrees. Using the term "substantially no hybridization does not render the claim indefinite. Applicant's terminology is commonly used and well understood in the art. "Substantially" is a term of degree used to modify absolute terms. *See e.g., Andrew Corp. v. Gabriel Electronics*, 847 F2d 819, 6 USPQ2d 2010 (Fed. Cir. 1988) ("substantially equal'); *Maitland Co. Inc. v. Terra First, Inc.*, 33 USPQ2d 1882, 1888 D. S.C. 1994) (substantially parallel). "Substantially no hybridization" does not mean exactly no hybridization. One of skill in the art would understand the claim language when read in light of the specification and the prior art, and the claim language need not be more precise that the subject matter permits. *See Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d at 1547, 221 USPQ. at 7. The skilled artisan would know the meaning of "substantially no

hybridization" and be able to distinguish it from "hybridization" under a particular set of hybridization and stringency conditions. Hence, these claims are neither vague nor indefinite.

Likewise, those skilled in the art recognize the meaning of "stringent conditions." One of skill in the art knows that various factors, including length and composition of nucleic acids, and ionic strength and temperature of wash conditions can be varied to generate conditions of either high or low stringency. Moreover, the ordinary skilled artisan would know how to vary these factors to generate conditions of high stringency, particularly in the case of probes recognized to contain conserved sequences, such as the *gag*, *pol* and *env* genes of Moloney-MLV. Ample details for adjusting hybridization conditions are well known in the art. (*see, e.g., Sambrook, et al.* (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, N.Y.).

Accordingly, the Applicant believes that the claims are definite as now drawn, that the rejection under 35 U.S.C. § 112, second paragraph is obviated and should be withdrawn.

IV. Conclusion

It is believed that the present application is in a condition for allowance which action is earnestly solicited. If the Examiner has any questions, he is invited to contact the

Respectfully submitted,

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Version of claims with markings to show changes made

1. (amended) A method for preparing a stable, retroviral packaging cell line for generation of human serum-resistant retroviral particles (RVP) which comprises

(a) introducing one or more packaging vectors into a non-primate mammalian cell line, wherein said cell line exhibits substantially no hybridization to a Moloney-MLV retrovirus *gag*, *pol*, and/or *env* probe under stringent washing conditions and is capable of producing human-serum-resistant RVP, and wherein said vectors, either singly or collectively, express a cellular targeting protein and retroviral *gag* and *pol* genes in amounts sufficient to package said RVP; and

(b) recovering said packaging cell line.

3. (amended) The method of Claim 1, wherein said cell line [is α-galactosyl positive] expresses galactose α (1,3) galactosyl epitopes and is not treated to reduce such expression.

4. (amended) The method of Claim 1 or [2] 42, wherein said cellular targeting protein is an amphotropic retroviral *env* protein, a xenotropic retroviral *env* protein, a polytropic retroviral *env* protein, a JSRV *env* protein, vesicular stomatitis virus G protein or transferrin.

10. (amended) Producer cells prepared by the method of Claim 6 or [7] 43.

14. (amended) The method of Claim 11 or [12] 44, wherein said cellular targeting protein is an amphotropic retroviral *env* protein, a xenotropic retroviral *env* protein, a polytropic retroviral *env* protein, a JSRV *env* protein, vesicular stomatitis virus G protein or transferrin.

20. (amended) Retroviral vector particles produced by the methods of any one of Claims 11, 12, 16 or [41] 45.